

1 GCTGTGGGA CCTCTCCAG CGCACGAACT CAGCCAACGA TTTCTGATAG ATTTTGGGA GTTGACCAG AGATGCAAG GGTGAAGGAG CGCTTCCTAC
CGACACCCCTT GGAGAGGTGC GCGTGTCTGA GTGGGTGCT AAAGACTATC TAAAAACCCT CAAACTGGTC TCTACGTTCC CCACCTCCTC GCGAAGGATG

101 CGTTAGGGA CTCTGGGAC AGAGCGCCCC GCGCGCTCTA TGGCCGAGGC AGGCTGGAC CCAGGACCCA GGACGGCTC GGAACCCATA CCATGGCCCC
GCAATCCCTT GAGACCCCTG TCTCGGGGG CCGGGGACT ACCGGCTCCG TCCACGCTG GGTCTGGGT CCTGCGGAG CCCTGGGTAT GTACCGGGC
MetalArg

201 GATCCCCAG ACCCTAAAGT TCGTGTCTG CATGTCTGG GTCTGTCTG CAGTCTAGC TTAATCTGCC ACCACTGCC GCGAGGAGGA AGTTCCCCAG
CTAGGGGTTT TGGGATTCA AGCAGCAGCA GTAGCAGGC CAGGACGAC GTACAGATCG AATGAGACGG TGGTACGGG CCGTCTCCT TCAAGGGGTC

4 IleProLys ThrLeuLysP heValValVa lIleValAla ValLeuLeuP roValLeuAl aTySerAla ThrThrAlaA rgGlnGluG l uValProGln

301 CAGACAGTG CCCCACAGCA ACAGAGGCAC AGCTTCAAG GGGAGGAGT TCCACGAGGA TCTCATAGAT CAGAACATAC TGGAGCCTGT AACCCGTGCA
GTCTGTACC GGGGTGTCTG TGTCTCCGT TCGAAGTTCC CCCTCCTCAC AGGTCTCCT AGAGTATCTA GTCTGTATG ACCTCGGACA TTGGGGCAGT

37 GlnThrVala laProGlnG l nGlnArgHis SerPheLysG lyGluGluCy sProAlaGly SerHisArg s erGluHisth rGlyAlaCy s AsnProCysThr

401 CAGAGGGTGT GGATTACACC AACGCTTCCA ACAATGAACC TTCTGTCTC CCATGTACAG TTGTAAATC AGATCAAAA CATAAAAAGT CCTGCACCAT
GTCTCCACA CCTAATGTG TTGGGAAGGT GTTACTTGG AAGAACGAAG GTTACATGTC AACATTAG TCTAGTTTTT GTATTTTCAA GGACGTGTA

71 GluGlyVa laspTyrThr AsnAlaSerA snAsnGluPr oSerCysPhe ProcysThrv alCysLysSe rAspGlnLys HisLysSers erCysThrMet

501 GACCAGAGC ACAGTGTGTC AGTGTAAGA AGGCACCTTC CGGAATGAAA ACTCCGAGA GATGTCCGG AGTGTAACA GTGCCCCTAG TGGGGAAGTC
CTGGTCTCTG TGTACACAG TCACATTCT TCCGTGGAAG GCCTTACTTT TGAGGGTCT CTACACGGCC TTCACATCGT CCACGGGATC ACCCTTCAG

104 ThrArgAsp ThrValCy sG l nCysLysG l uGlyThrPhe ArgAsnGluA snSerProG l uMetCysArg LysCysSerA rgCysProSe rGlyGluVal

601 CAAGTCAGTA ATTGTACGTC CTGGGATGAT ATCCAGTGTG TTGAAGAATT TGGTGCCAAT GCCACTGTG AAACCCCGC TGTGAAGAG ACAATGAACA
GTTACAGTCA TAAATGCAG GACCTACTA TAGGTACAC ACCTTCTTAA ACCACGGTTA CCGTGACACC TTTGGGGTCG ACGACTTCTC TGTACTTGT

137 GlnValSerA snCysThrSe rTrpAspAsp l leGlnCysV alGluGluP h eGlyAlaAsn AlaThrValG luThrProAl aAlaGluGlu ThrMetAsnThr

701 CCAGCCCGG GACTCCTGCC CCAGCTGCTG AAGAGACAAT GAACACCCAG CCAGGACTC CTGCCCCAGC TGCTGAAGAG ACAATGACCA CCAGCCCCGG
GGTCGGGGCC CTGAGGACGG GGTGACGAC TTCTCTGTTA CTGTGTGTCG GTCCCTGAG GACGGGGTCG ACGACTTCTC TGTACTGTTT GGTCGGGGCC

171 SerProG l yThrProAla ProAlaAlaG luGluThrMe tAsnThrSer ProGlyThrP roAlaProAl aAlaGluGlu ThrMetThrT hrSerProGly

FIG. 1A-1

801 GACTCCTGCC CCAGCTGCTG AAGAGACAAT GACCAACCAGC CCGGGGACTC CTGCCCCAGC TGCTGAAGAG ACAATGACCA CCAGCCCGGG GACTCCTGCC
CTGAGGACGG GGTCCAGCAC TTCTCTGTTA CTGGTGTTCG GCGCCCTGAG GACGGGGTGC AGACTTCTC TGTTACTGGT GGTCCGGGCC CTGAGGACGG
204 ThrProAla ProAlaAlaG luGluThrMe tThrThrSer ProGlyThrp roAlaProAl aAlaGluGlu ThrMetThrt hrSerProGl yThrProAla
901 TCTTCTCATT ACCTCTCATG CACCATCGTA GGGATCATAG TTCTAATTGT GCTTCTGTAT GAAAGACTTC ACTGTGGAAG AAATTCCTTC
AGAAGAGTAA TGGAGAGTAC GTGGTAGCAT CCTAGTATC CCAAGACTAA CGAAGACTAA CACAAACAAA CTTTCTGAAG TGACACCTTC TTAAAGGAAG
237 SerSerHst yrLeuSerCy sThrIleVal GlyIleIleVal lleuLeuIle ValpheVal
1001 CTTACCTGAA AGGTTACGGT AGGCGCTGGC TGAGGGGGGG GGGCGCTGGA CACTCTCTGC CCGCTCTCCC TCTGCTGTGT TCCACACAGC AGAAACGCCT
GAATGGACTT TCCAAGTCCA TCCGCGACCG ACTCCGGCCC CCGCGGACCT GTGAGAGAGC GGACGGAGGG AGACGACACA AGGCTGTCTG TCTTTGCGGA
1101 CCCCCTGCCC CAAAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA AAAA
CGGGACGGG GTTTTTTTTT TTTTTTTTTT TTTTTTTTTT TTTTTTTTTT TTTTTTTTTT TTTTTTTTTT TTTTTTTTTT TTTTTTTTTT

FIG. 1A-2

1 GCTGTGGGAA CCTCTCCACG CGACGAACT CAGCCAAACGA TTTCTGATAG ATTTTGGGA GTTGTACCAG AGATGCAAGG GGTGAAGGAG CGCTTCCTAC
CGACACCCCT GGAGAGGTGC GCGTGTGA GTCCGTGGA TAAACCTC AAAGACTATC TAAACCTC CAAACTGGTC TCTACGTTCC CCACCTCTCC GCGAAGGATG
MetGlnGl yValLysGlu ArgPheLeuPro
101 CGTTAGGGAA CTCTGGGGAC AGAGCGCCCC GCGCGCCTGA TGGCCGAGGC AGGGTGCAGC CCAGGACCCA GGACGGCGTC GGAACCATTA CCATGGCCCG
GCAATCCCTT GAGACCCCTG TCTCGCGGG TCTCGCGGGT CCGCGGGACT ACCGGCTCCG TCCACAGCTG GGTCTGGGT CCTGCCGAG CCCTTGGTAT GTACCGGGC
-30 LeuGlyAs nserGlyAsp ArgAlaProA rgProProAs pGlyArgGly ArgValArgp roArgThrgl nAspGlyVal GlyAsnHist hrMetAlaArg
201 GATCCCAAG ACCCTAAAGT TCGTCTCGT CATCGTCGG GTCTGTCTGC CAGTCTTAGC TTACTCTGCC ACCACTGCC GGCAGGAGGA AGTCCCCAG
CTAGGGGTTT TGGGATTCA AGCAGACGA GTAGCAGCG CAGGACGACG GTCAGGATCG AATGAGACGG TGTGACGG CCGTCTCTCT TCAAGGGTC
4 IleProLys ThrLeuLysp heValValva lleValAla ValLeuLeup roValLeuAl aTySerAla ThrThrAlaA rgGlnGluGl uValProGln
301 CAGACAGTGG CCCCACAGCA ACAGAGGAC ACCTTCAAG GGGAGGAGTG TCCAGCAGGA TCTCATAGAT CAGAACATAC TGGAGCCTGT AACCCGTGCA
GTCTGTCAAC GGGGTGTCGT TGTCTCCGT TGTCTCCGT TCGAAGTTCC CCGTCTCAC AGGTCTCTT AGAGTATCTA GTCTTGTATG ACCTCGGACA TTGGGCACGT
37 GlnThrVala laProGlnGl nGlnArgHis SerPheLysG lyGluGluCy sproAlaGly SerHisArgS erGluHisTh rGlyAlaCys AsnProCysThr

FIG. 1B-1

[illegible]

FIG. 1B-2

Apo2 1 -----MEQRGQNAFAASGARRRHGPGPREARGARPGRLVPKTLVL
 Apo2DcR 1 -----MARIPKTLKFVV
 DR4 51 GRGALPTSMGQHGPSARARAGRAPGERPAREASPRLRVHKTFKFVVGVV

Apo2 41 VVAAVLLLVSAESALITQODLAPQORAAPOOKRSSPSEGLCPPGHHSIED
 Apo2DcR 13 VIVAVLLPVILAYSATTARQEEVPQOTVAPQOQRHSFKGEECPAGSHRSEH
 DR4 101 LQVVPSSAATIK-----LHDQSIGTQOWEHSPLGELCPPGSHRSEH

Apo2 91 GRDCISCKYGGDYSTHWNDLLFCLRCTRCDSGEVELSPCTTTRNTVCQCE
 Apo2DcR 63 TGACNPECTEGVDYTNASNNEPSCFPCTVCKSDQKHSSCTMTRDITVCQCK
 DR4 142 PGACNRCTEGVGYTNASNNEFACLPCTACKSDEEERSPCTTTRNTACQCK

Apo2 141 EGTFREEDSPEMCRKCRITGCPRGMVKVGDCPTWSDIECVHKE-----
 Apo2DcR 113 EGTFRNENSPEMCRKCSR-CPSGEVQVSNTSWDDIQCVE-EFGANATVE
 DR4 192 EGTFRNDNSAEMCRKCRSTGCPRGMVKVKDCTPWSIDIECVHKE-----

Apo2 -----
 Apo2DcR 161 TPAAEETMNTSPGTPAPAAEETMNTSPGTPAPAAEETMTTSPGTPAPAAE
 DR4 -----

Apo2 183 -----SGIILIGVTVAAVVLLIVAVEV---
 Apo2DcR 211 ETMTTSPGTPAPAAEETMTTSPGTPASSHYLSCTIVGIIIVLLIVLLIVFV
 DR4 234 -----SGNGHNIWVILLVVTLVVPILLIVAV-LIVC

Apo2 203 CKSLLWKKVL PYLKGICSGGGGDPFRVDRSSQRPGAEDNVLNEIVSILQP
 DR4 262 CCIGSGCGGDPKCMDRVCFWRLGLLRGPGAEDNAHNEILSNADSLSTFVS

Apo2 253 TQVPEQEMEVOEPAEPTGVNMLSPGESEHLLPAAEAERSQRRRLLVPANE
 DR4 312 ----EQQMESQEPADLTGVTVQSPGEAQCLLGPAEAEGSQRRRLLVPANG

Apo2 303 G D P T E T L R Q C F D D F A D L V F F D S W E F L M R K L G L M D N E I R V A K A E A A G H - - R
 DR4 358 A D P T E T I M L F F D K F A N I V F F D S W D Q L M R Q L D L T K N E I D V V R A G T A G P - - G
 Apo3/DR3 338 V M D A V P A R R W K E F V R T L G L R E A E I E A V E V E I - G R F - R
 TNFR1 322 V V E N V P L R W K E F V R R L G L S D H E I D R I E L O N - G R C L R
 CD95 220 I A G V H T L S Q V K G F V R K N G V N E A K I D E I K N D N - V Q D T A

Apo2 351 D I L Y I M L I K W V N K T G R - D A S V H T L L D A E T L G E R L A K Q K I E D H L L S S G K F
 DR4 406 D A L Y A M L M K W V N K T G R - N A S I H T L L D A L E R M E E R H A K E K I Q D L L V D S G K F
 Apo3/DR3 374 D Q Q Y E M L K R W R Q Q Q P - - - A G L G A V Y A A L E R M G L D G C V E D L R S
 TNFR1 358 E A Q Y S M L A T W R R R T E R R E A T L E L L G R V L R D M D L L G C L E D I E E
 CD95 256 E Q K V Q I L R N W H Q L H G K K E A Y - D T L I K D L K K A N L C T L A E K I Q T

Apo2 400 M Y L E G N A D S A L S
 DR4 455 I Y L E D G T G S A V S L E

FIG. 2

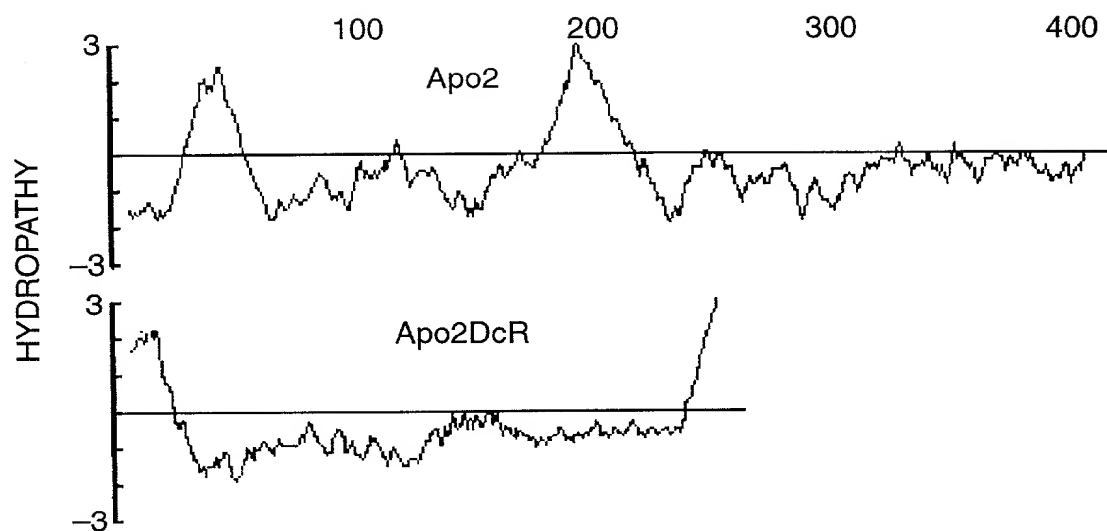


FIG._3

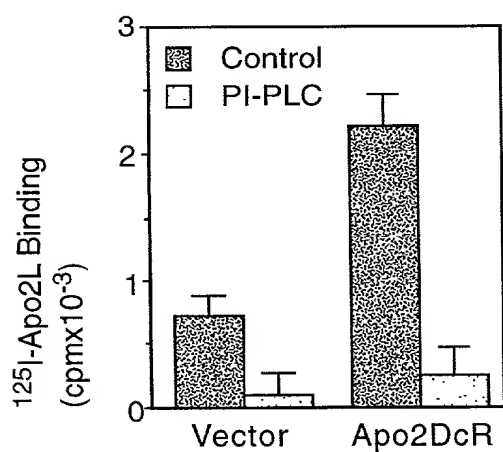


FIG._4

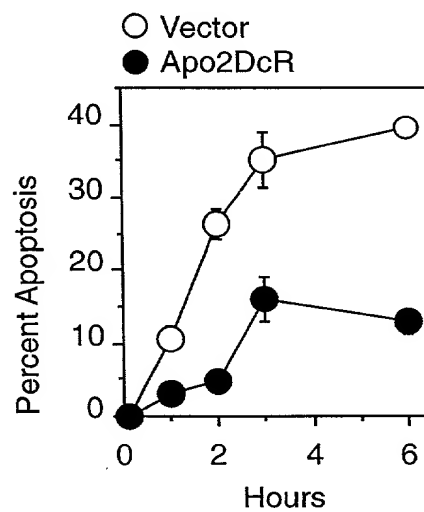


FIG._5

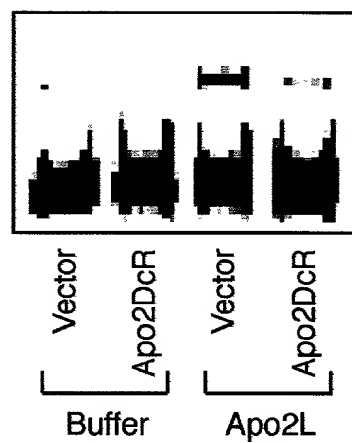


FIG._6

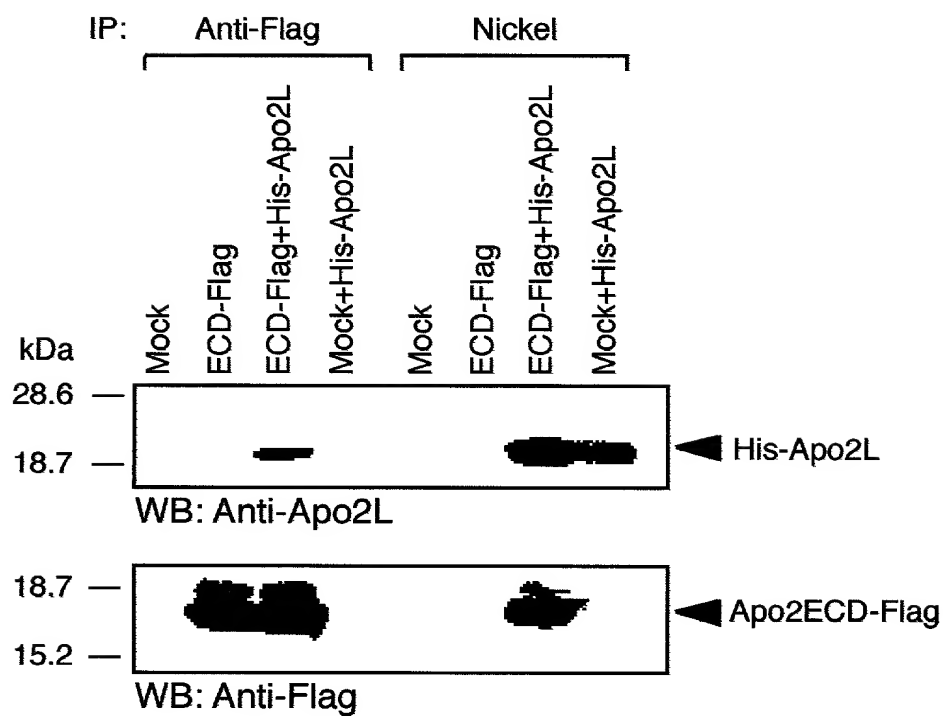


FIG._10

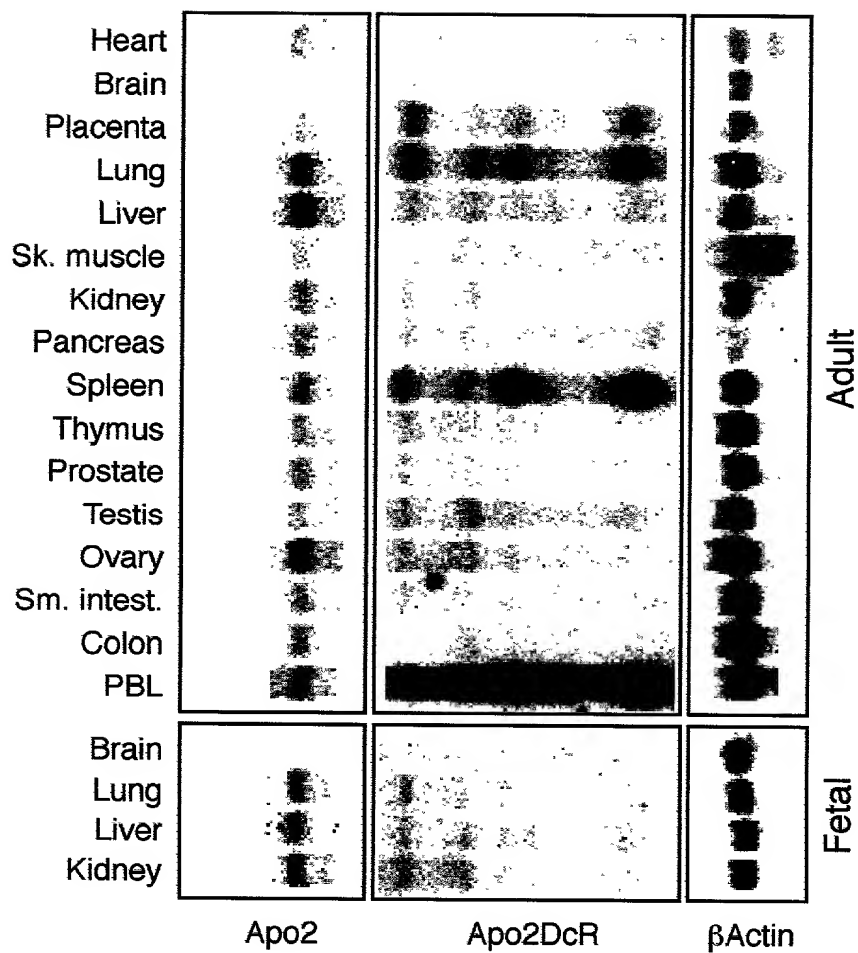


FIG. 7

+

1 CCCACGGCGT CGCATAAATC AGCAGCGCGC CGGAGAACCC CGCAATCTCT GCGCCACAA ATACACCGA CGATGCCCGA TCTACTTTAA GGGCTGAAAC
GGGTGGCGAG CGGTATTAG TCGTGGCGCG GCCTCTGGG CGGTAGAGA CCGGGGTCTT TTAATCTGGT GCTACGGGCT AGATGAAATT CCGGACTTTG

101 CCACGGGGCT GAGAGACTAT AAGAGCGTTC CCTACCGCCA TGAACAACG GGGACAGAAC GCCCGGGCG CTTCCGGGGC CCGGAAAAGG CACGGCCCCAG
GGTGGCCCGA CTCTCTGATA TTCTCGCAAG GGATGGCGGT ACCTGTGTC CCCTGTCTTG CCGGGCGGC GAAGCCCCC GGCCTTTTCC GTGCCGGGTC

1 M etGluGlnAr gGlyGlnAsn AlaProAla laSerGlyAl aArgLysArg HisGlyProGly

201 GACCCAGGGA GCGCGGGGA GCCAGGCCCT GGTCCGGGT CCCCAGACC CTTGTCTCTG TGTCTGGCG GGTCTGCTG TTGCTCTCAG CTGAGTCTGC
CTGGTCTCCT CCGCGCCCT CCGTCCGGAC CCGAGGCCCA GGGTCTCTG GAACACGAG AACAGCGCG CCAGGACGAC AACACAGATC GACTCAGACG

22 ProArgG1 uAlaArgGly AlaArgProG lYLeuArgVa lProLysThr LeuValLeuV alValAlaAl aValLeuLeu LeuValSerA laGluSerAla

301 TCTGATCACC CAACAAGACC TAGCTCCCCA GCAGAGAGCG GCCCCACAAC AAACAGAGTC CAGCCCCCTCA GAGGGATTGT GTCCACCTGG ACACCATATC
AGACTAGTGG GTTGTCTG ATCAGGGGCT CGTCTCTCG CCGGGTGTG TTTCTCTCCAG GTCCGGGAGT CTCCTTAACA CAGGTGGACC TGTGGTATAG

55 LeuileThr GlnGlnAspL euAlaProG1 nGlnArgAla AlaProGlnG lNlysArgSe rSerProSer GluGlyLeuC ysProProG1 yHisHisile

401 TCAGAAGACG GTAGAGATTG CATCTCCTGC AAATATGGAC AGGACTATAG CACTCACTGG AATGACCTCC TTTTCTGCTT CCGCTGCACC AGGTGTGATT
AGTCTTCTGC CATCTCTAAC GTAGAGGACG TTTATACCTG TCCTGATATC GTGAGTGACC TTACTGGAGG AAAAGACGAA CCGGACGTGG TCCACACTAA

88 SerGluAspG lyArgAspCy sIleSerCys LysTyrGlyG lNAspTyrSe rThrHisTrp AsnAspLeuL euPheCysLe uArgCysThr ArgCysAspSer

501 CAGGTGAAGT GGAGCTAAGT CCTGACCA CCCTGCACCA CGACCAGAAA CACAGTGTGT CAGTGCGAAG AAGGCACCTT CCGGGAAGAA GATTCTCTG AGATGTGCCG
GTCCACTTCA CCTCGATTCA GGGACGTGGT GCTGGTCTTT GTGTACACA GTACCGCTTC TTCCGTGGAA GGCCTTCTT CTAAGAGGAC TCTACACGGC

122 GlyGluVa lGluLeuSer ProCysThrT hrThrArgAs nThrValCys GlnCysGluG luGlyThrPh eArgGluGlu AspSerProG luMetCysArg

601 GAAGTGCCCG ACAGGGTGTG CCAGAGGGAT GGTCAAGTTC GGTGATTGTA CACCCTGGAG TGACATCGAA TGTGTCCACA AAGAATCAGG CATCATCATA
CTTCACGGCG TGTCCACACAG GGTCTCCCTA CCAGTTCACG CCACATAACAT GTGGGACCTC ACTGTAGCTT ACACAGGTGT TTCTTAGTCC GTAGTAGTAT

155 LysCysArg ThrGlyCysP roArgGlyMe tValLysVal GlyAspCysT hrProTrpSe rAspIleGlu CysValHisL ysGluSerG1 yIleIleIle

701 GGAGTCACAG TTGCAGCCGT AGTCTTGATT GTGGCTGTGT TTGTTTGCAA GTCTTTACTG TGAAGAAGG TCCTTCTCTTA CCTGAAAGG ATCTGCTCAG
CCTCAGTGTG AACGTCCGCA TCAGAACTAA CACCGACACA AACAAAGGT CAGAAATGAC ACCTTCTTTC AGGAAGGAAT GGACTTTCCG TAGACGAGTC

188 GlyValThrV alAlaAlaVa lValLeuIle ValAlaValP heValCysLy sSerLeuLeu TrpLysLysV alLeuProTy rLeuLysGly IleCysSerGly

FIG. 8A-1

801 GTGGTGGTGG GGACCCCTGAG CGTGTGGACA GAAGCTCACA ACGACCTGGG GCTGAGGACA ATGTCCTCAA TGAGATCGTG AGTATCTTGC AGCCCAACCA
 CACCACCACC CCTGGGACTC GCACACCTGT CTTGAGTGT TCTGGACCC CGACTCCTGT TACAGGAGTT ACTCTAGCAC TCATAGAACG TCGGGTGGGT
 222 GlyGlyGly yAspProGlu ArgValAspA rgSerSergl nArgProGly AlaGluAspA snValLeuAs nGluIleVal serIleLeuG lnProThrGln
 901 GGTCCCTGAG CAGGAAATGG AAGTCCAGGA GCCAGCAGAG CCAACAGGTG TCAACATGTT GTCCCCCGGG GAGTCAGAGC ATCTGCTGGA ACCGGCAGAA
 CCAGGGACTC GTCCTTTACC TTCAGGTCCT CGGTCGTCTC GGTGTCCAC AGTTGTACAA CAGGGGGCCC CTCAGTCTCG TAGACGACCT TGGCCGTCTT
 255 ValProGlu GlnGluMetG luValGlnG luProAlaGlu ProThrGlyV alasnMetLe uSerProGly GluSerGluH isLeuLeuG l uProAlaGlu
 1001 GCTGAAAGGT CTCAGAGGAG GAGGCTGCTG GTTCCAGCAA ATGAAGGTGA TCCCACTGAG ACTCTGAGAC AGTGCTTTCGA TGACTTTTGA GACTTGGTGC
 CGACTTTCCA GAGTCTCCTC CTCCGACGAC CAAGGTCGTT TACTTCCACT AGGGTCACTC TGAGACTCTG TCACGAAAGCT ACTGAAACGT CTGAACCCACG
 288 AlaGluArgS erGlnArgAr gArgLeuLeu ValProAlaA snGluGlyAs pProThrGlu ThrLeuArgG lncysPheAs pAspPheAla AspLeuValPro

FIG.-8A-2

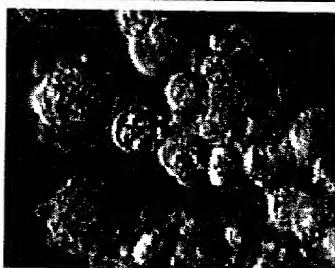
FIG. 9

1 MEORQONAPAAAGARKRHGPPREARGARPGRLVPPKTLVLVVAALLVSAESALITQQD
61 LAPQRAAPQKKRSPSEGLCPPGHHISEDGRDCISCKYQDYSTHWNLLFCRLCTRCD
121 SGEVELSPCTTTRNTVQCCEGTFREEDSPEMCRKCRGTGCPRGMVKVGDC¹TPWSDIECVH
181 KESGIIIGVTVAAVLIVAVFCKSLMKKVLPLYLKGICSGGGDPERVDRSSQRPGEAD
241 NVLNEIVSILQTPQVEQEMEVOEPAEPTGVNMLSPGESEHLLPEAAERSQRRRLLVPA
301 NEGDPTE²TLRQCDDFADLV³PFDSWEPLMRKLGIMDNEIKVAKAAEAGHRD⁴TY⁵TMLIKW
361 VNKTGRDASVHTLLDALETGLERLAKQKIEDHLLSSCKFMYLEGNADSAIS

Vector



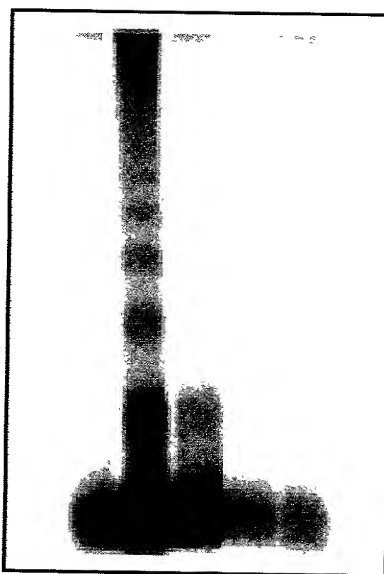
Apo2



Apo2+CrmA



FIG. 11A



Vector

Apo2

Apo2+CrmA

Apo2+DEVD

Apo2+ZVAD

FIG. 11B

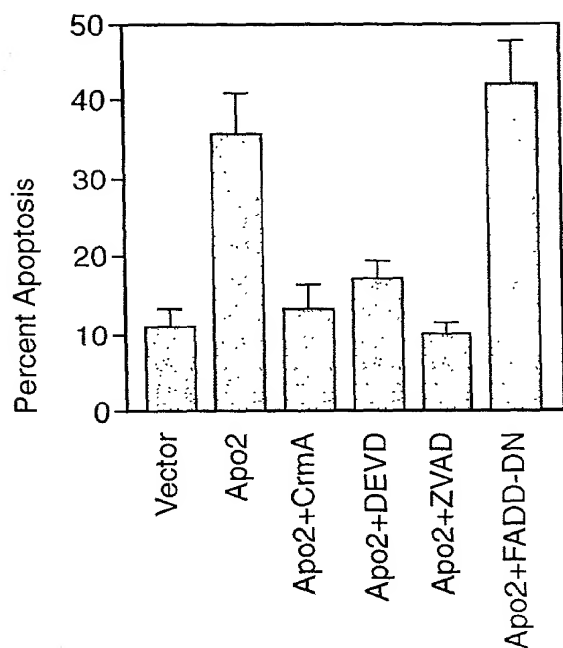


FIG. 11C

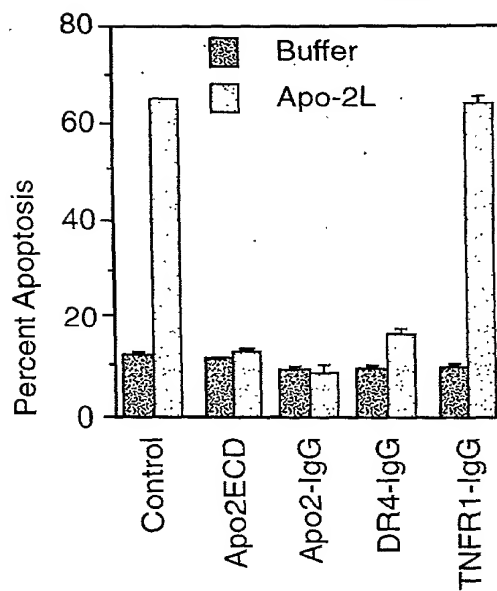


FIG. 11D

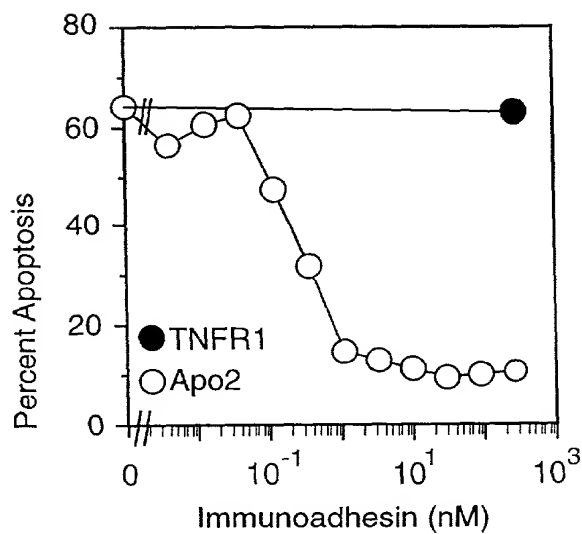


FIG. 11E

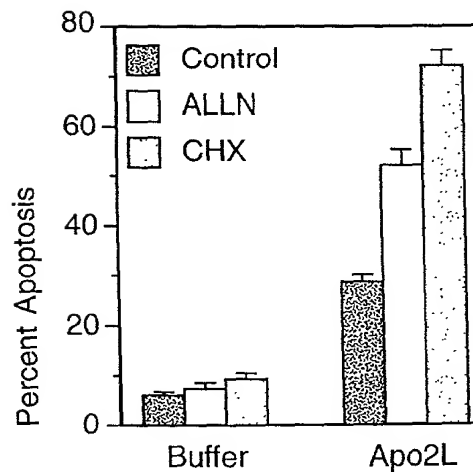
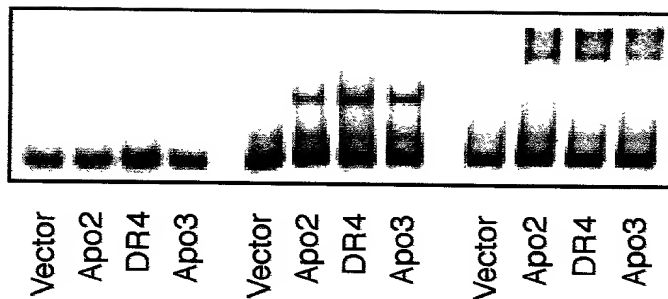


FIG. 12C

Unlabelled probe	+	+	+	+	-	-	-	-	-	-	-	-
Labelled probe	+	+	+	+	+	+	+	+	+	+	+	+
Anti-p65	-	-	-	-	-	-	-	-	+	+	+	+

FIG._12A



Unlabelled probe	-	-	-	-	-	-
Labelled probe	+	+	+	+	+	+
Anti-p65	-	-	-	-	-	-

FIG._12B

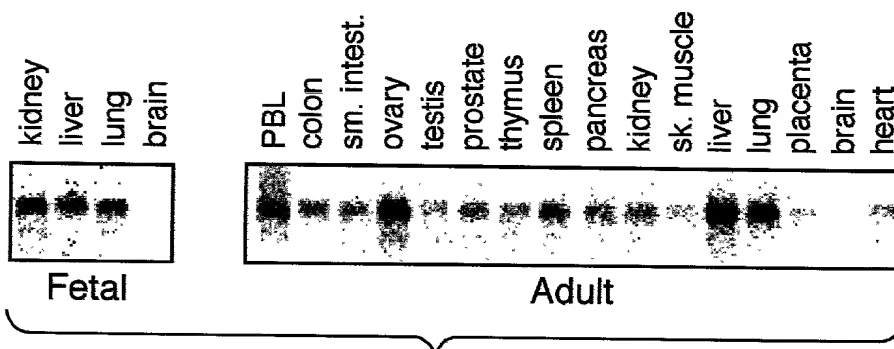
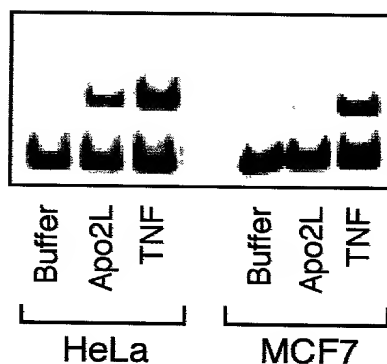


FIG._13